PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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DUE DATE:	–
FORMALITIES:	THV
PAT. OFF:	TB ✓
ON DB:	–
CASE NO:	PA0304-PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing (day/month/year) 15.07.2005

Applicant's or agent's file reference
PA0304

IMPORTANT NOTIFICATION

International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/GB 03/03876	08.09.2003	02.04.2003

Applicant
AMERSHAM BIOSCIENCES UK LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:

European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
PA0304		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB 03/03876	08.09.2003	02.04.2003
International Patent Classification (IPC) or both national classification and IPC		
G06K9/00		
Applicant		
AMERSHAM BIOSCIENCES UK LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06.10.2004	15.07.2005
Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Koch, A Telephone No. +31 70 340-3828

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/03876

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-48 as originally filed

Sequence listings part of the description, Pages

1, 2 as originally filed

Claims, Numbers

1-28 as originally filed

Drawings, Sheets

1/10-10/10 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-28
	No:	Claims	1
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-28
Industrial applicability (IA)	Yes:	Claims	1-28
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 01/11341 A (SHOPOFF RANDALL O ;BRIGHT GARY (US); CELLOMICS INC (US); LAPETS OL) 15 February 2001 (2001-02-15)

D2: US-A-5 856 665 (GOUGH DAVID ET AL) 5 January 1999 (1999-01-05)

1. The application contains the independent claims 1, 26, 27 and 28, claims 1-25 referring to methods and claims 26-28 referring to products.

2. Claims 1 and 26-28 do not comply with the requirements of Articles 33(1) and (2) PCT, the reasons being as follows:

2.1 The technical features of claims 1 and 28 are all anticipated by document D1 disclosing automatic screening and imaging of cells by use of two or more luminescent reporters, the method being performed under the control of a computer with suitable software. Regarding claim 1, this document describes in example 9, page 59, line 15-p. 63, l. 33:

A method of determining cell cycle phase data for cells comprising at least one luminescent reporter capable of emitting radiation, the at least one luminiscent reporter comprising a first luminescent reporter which is capable of being indicative of at least one cell cycle phase, said method comprising:

storing classification information for classifying individual cells into different cell cycle phases using an automated classification process;

receiving image data to identify object areas in the image data which correspond to individual cells;

analyzing said image data, on the basis of said identified object areas, to determine, for a selected cell, one or more measurements including a measurement of a parameter relating to at least one cytoplasmic component of the cell; and

applying said classification information to said measurements to classify the selected cell into a selected one of a plurality of sub-populations of cells, each sub-population having cells in a different cell cycle phase.

D1 describes a method for automatically screening cells and determining the location, organisation and integrity of luminescently-labelled microtubules in living cells at all stages of the cell cycle by high content screening (HCS) (p. 60, l. 10-12 with p. 59, l. 16-22). In this method an image of the nucleus and the cytoplasma is provided, the area of the nucleus and of the cytoplasma is identified in the image (p. 62, l. 10-17), and locations with increased luminescent activity within the cell and as well as data on the microtubule morphology are provided (p. 62, l. 7-19 with p. 60, l. 7-12); evidently cytoplasmic components are also imaged in this method and used for evaluating the distribution of luminescent microtubule-labelling molecules within cells, which have been contacted with a test compound, in space and time (p. 59, l. 16-22). Since the skilled person would know that, in particular, microtubule organisation, is suitable for distinguishing different phases of the cell cycle, the identification of different phases of the cell cycle by this method of example 9 of D1 is considered implicitly disclosed.

2.2 Even if the applicant would argue that it is not common general knowledge of the skilled person that microtubule organisation is suitable for distinguishing different phases of the cell cycle, and that therefore claim 1 has to be considered novel over D1, claim 1 would not comply with Article 33(1) and (3) PCT, the reasons being as follows:
In example 10 of the same document (D1) it is explicitly disclosed that "microtubule spindle formation" is characteristic for mitosis of cells and thus for the determination of the mitotic index as the percentage of dividing cells withing a given population (p. 64, l. 10-14 and p. 65, l. 5-19). Thus the technical problem, i.e. the determination of the cell cycle phase (namely mitosis) for a cell, and the solution, namely determination of the microtubule organisation ("microtubule spindle formation"), all by means of a similar automatic luminescent imaging method as it is also described in more detail in example 9, are explicitly described.
Therefore the skilled person would use the imaging method of example 9 as a technical alternative to the imaging method of example 10 also for determining cell cycle data and thus arrive at a method according to claim 1 without an inventive step being involved.

2.3 The technical features which claims 26-28 have over claim 1 are also known from

example 10 of D1, for the same or a similar technical purpose, since D1 discloses automatic screening and imaging of cells by use of two or more luminescent reporters, the method being performed under the control of a computer with suitable software (page 65, line 5-p. 66, l. 12 with p. 8, l. 23-p. 10, l. 3 and p. 13, l. 1-p. 14, l. 24 of D1). In example 10 of D1, this method is clearly applied to evaluate cell cycle phase data (to identify mitotic cells). Therefore claims 26-28 do not comply with the requirements of Articles 33(1) and (3) PCT of an inventive step.

3. The technical features of dependent claims 2-11 and 16-25 are likewise known from document D1 for the same or a similar technical purpose, so that these claims do not comply with the requirements of Articles 33(1) and (3) PCT of an inventive step.

4. Claims 12-15 do not meet the requirements of Articles 33(1) and (3) PCT, the reasons being as follows:
The features which claims 12-15 have over the closest prior art document D1 concern the links between the intensity of the nuclear luminescence signal and the cell cycle phase. These links are also disclosed in D2 for the same or a similar technical purpose (col. 20, l. 66-col. 22, l. 52), D2 describing an "operator-independent image cytometer". It is not required that D2 explicitly describes a measurement relating to a cytoplasmic component since such a measurement is already known from example 9 of D1 which is considered the closest prior art document.

5. None of the claims seems to comply with the requirements of Articles 33(1) and (3) PCT.